

The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (withdrawn) A method of inhibiting osteoclast generation, the method comprising administering to a patient in need thereof a therapeutic composition comprising a recombinant soluble RANK polypeptide.

2. (withdrawn) The method of claim 1, wherein the soluble RANK is encoded by a DNA selected from the group consisting of:

(a) a DNA encoding a protein having an amino acid sequence as set forth in SEQ ID NO:2, wherein the protein has an amino terminus selected from the group consisting of an amino acid between amino acid 1 and amino acid 33, inclusive, of SEQ ID NO:2, and a carboxy terminus selected from the group consisting an amino acid between amino acid 196 and amino acid 616, inclusive;

(b) a DNA encoding a protein having an amino acid sequence as set forth in SEQ ID NO:5, wherein the protein has an amino terminus selected from the group consisting of an amino acid between amino acid 1 and amino acid 30, inclusive, of SEQ ID NO:5, and a carboxy terminus selected from the group consisting an amino acid between amino acid 197 and amino acid 625, inclusive;

(c) DNA molecules capable of hybridization to the DNA of (a) or (b) under stringent conditions, and which encode RANK polypeptides that bind RANKL; and

(d) DNA molecules encoding fragments of proteins encoded by the DNA of (a), (b) or (c), wherein the fragments of RANK polypeptides bind RANKL.

3. (withdrawn) The method of claim 2, wherein the RANK is at least about 80% identical in amino acid sequence to native RANK.

4. (withdrawn) The method of claim 3, wherein the RANK further comprises a polypeptide selected from the group consisting of an immunoglobulin Fc domain, an immunoglobulin Fc mutein, a FLAGTM tag, a peptide comprising at least about 6 His residues, a leucine zipper, and combinations thereof.

5. (currently amended) A method of inhibiting RANKL-induced osteoclastogenesis in a patient in need thereof, comprising administering to said patient a soluble RANK polypeptide composition, wherein said patient suffers from a condition selected from the group consisting of bone cancer, multiple myeloma, melanoma and breast cancer, and further wherein the soluble RANK polypeptide is capable of binding to a RANKL polypeptide that consists of amino acids 1-317 of SEQ ID NO:8 and is selected from the group consisting of:

(a) a polypeptide ~~encoded by a DNA that encodes a protein~~ comprising amino acids 33-196 of SEQ ID NO:2;

(b) a polypeptide encoded by a DNA that is capable of hybridizing to a DNA consisting of the nucleotide sequence shown in SEQ ID NO:1 under stringent conditions, wherein stringent conditions comprise prewashing in 5 x SSC, 0.5% SDS, 1.0 mM EDTA, pH 8.0, hybridizing at 63°C in 6 x SSC and washing in 3 X SSC at 55 °C;

(c) a polypeptide that is at least ~~80%~~ 90% identical in amino acid sequence to a RANK polypeptide comprising amino acids 33-213 of SEQ ID NO:2; and

(d) a polypeptide comprising amino acids 33-213 of SEQ ID NO:2, and

further wherein said composition is administered in an amount sufficient to inhibit RANKL-induced osteoclastogenesis in said patient.

6-8. (canceled)

9. (currently amended) The method of claim 5, wherein the soluble RANK polypeptide further comprises a polypeptide selected from the group consisting of an immunoglobulin Fc domain, an immunoglobulin Fc mutein, a FLAG™ tag, a peptide comprising at least 6 His residues, a leucine zipper, and combinations thereof.

10. (canceled)

11. (currently amended) The method of claim 9, wherein the soluble RANK polypeptide comprises an amino acid sequence that is at least ~~80%~~ 90% identical in amino acid sequence to amino acids 33-213 of SEQ ID NO:2.

12. (canceled)

13. (currently amended) A method of inhibiting RANKL-induced osteoclastogenesis in a patient in need thereof, said method comprising administering to said patient a composition comprising a recombinant soluble RANK polypeptide, wherein said patient suffers from a condition selected from the group consisting of squamous cell carcinoma, lung cancer, prostate cancer, hematologic cancer, head and neck cancer and renal cancer, and further wherein the soluble RANK polypeptide is capable of binding to a RANKL polypeptide that consists of amino acids 1-317 of SEQ ID NO:8 and is selected from the group consisting of:

(a) a polypeptide ~~encoded by a DNA that encodes a protein~~ comprising amino acids 33-196 of SEQ ID NO:2;

(b) a polypeptide encoded by a DNA that is capable of hybridizing to a DNA consisting of the nucleotide sequence shown in SEQ ID NO:1 under stringent conditions, wherein stringent conditions comprise prewashing in 5 x SSC, 0.5% SDS, 1.0 mM EDTA, pH 8.0, hybridizing at 63°C in 6 x SSC and washing in 3 X SSC at 55 °C;

(c) a polypeptide that is at least ~~80%~~ 90% identical in amino acid sequence to amino acids 33-213 of SEQ ID NO:2; and

(d) a polypeptide comprising amino acids 33-213 of SEQ ID NO:2, and further wherein said composition is administered in an amount sufficient to inhibit RANKL-induced osteoclastogenesis in said patient.

14. (canceled)

15. (currently amended) The method of claim 13, wherein the soluble RANK polypeptide comprises an amino acid sequence that is at least ~~80%~~ 90% identical in amino acid sequence to amino acids 33-213 of SEQ ID NO:2.

16. (previously presented) The method of claim 13, wherein the soluble RANK polypeptide further comprises one or more polypeptides selected from the group consisting of an immunoglobulin Fc domain, an immunoglobulin Fc mutein, a FLAGTM tag, a peptide comprising at least 6 His residues and a leucine zipper.

17. (withdrawn) A method according to claim 4, wherein the further polypeptide is selected from the group consisting of an immunoglobulin Fc domain comprising an amino acid sequence as shown in SEQ ID NO:3 and a leucine zipper comprising an amino acid sequence as shown in SEQ ID NO:6.

18. (previously presented) A method according to claim 9, wherein the further polypeptide is selected from the group consisting of an immunoglobulin Fc domain comprising the amino acid sequence as shown in SEQ ID NO:3 and a leucine zipper comprising the amino acid sequence as shown in SEQ ID NO:6.

19. (canceled)

20. (previously presented) A method according to claim 16, wherein the further polypeptide is selected from the group consisting of an immunoglobulin Fc domain having the amino acid sequence as shown in SEQ ID NO:3 and a leucine zipper having the amino acid sequence as shown in SEQ ID NO:6.

21. (withdrawn) A method according to claim 1, wherein the soluble RANK polypeptide comprises amino acids 34 through 196 of SEQ ID NO:2.

22-24. (canceled)

25. (previously presented) A method according to claim 18, wherein the soluble RANK polypeptide consists of amino acids 30-213 of SEQ ID NO:2 fused with the amino acid sequence as shown in SEQ ID NO:3.

26. (previously presented) A method according to claim 20, wherein the soluble RANK polypeptide consists of amino acids 30-213 of SEQ ID NO:2 fused with the amino acid sequence as shown in SEQ ID NO:3.